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Development of Advanced Multi-Modality Radiation Treatment Planning Software

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DEVELOPMENT OF ADVANCED MULTI-MODALITY RADIATION TREATMENT PLANNING SOFTWARE

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SUMMARY

The Idaho National Engineering and Environmental Laboratory (INEEL) has long been active in development of advanced Monte-Carlo based computational dosimetry and treatment planning methods and software for advanced radiotherapy, with a particular focus on Neutron Capture Therapy (NCT) and, to a somewhat lesser extent, Fast-Neutron Therapy. The most recent INEEL software ~~product~~ system of this type is known as SERA, Simulation Environment for Radiotherapy Applications[1]. SERA is at a mature level in its life cycle, it has been licensed for research use worldwide, and it has become well established as a computational tool for research. However, along with its strengths, SERA also has some limitations in its structure and computational methodologies. More specifically, it is optimized only for neutron-based applications. Although photon transport can be computed with SERA, the simplified model that is used is designed primarily for photons produced in the neutron transport process. Thus SERA is not appropriate for applications to, for example, standard external-beam photon radiotherapy, which is by far more commonly used in the clinic than neutron based therapy.

~~On the other hand~~At the same time, workers at Lawrence Livermore National Laboratory (LLNL)~~,~~ ~~the developers~~have developed the ~~of the well known~~ PEREGRINE Monte Carlo code system, optimized for photon and electron therapy ~~photon and electron therapy~~[2] ~~have focused their efforts on software that is optimized for external beam photon and electron therapy~~. Thus, as a

logical next step in the development of modern radiotherapy

planning tools to support the most advanced research, INEEL and LLNL have recently launched a new project to collaborate in the development of a "next-generation" multi-modality treatment planning software system. This effort will draw on the combined experience of the two laboratories in their respective areas of interest to produce a new system that will be useful for all modern forms of radiotherapy. This article provides summary descriptions of the SERA and PEREGRINE systems, followed by a discussion of the more recent new developmental effort being undertaken by INEEL and LLNL.

I. INEEL DEVELOPMENTS IN COMPUTATIONAL MEDICAL RADIATION DOSIMETRY

Figure 1 shows, on the left-hand side, a ~~some~~ history of the medical treatment planning software developmental effort at the INEEL, which has been focused almost entirely on neutron-based applications.

In the 1980s, it became apparent that new computational methods were required to support large animal model preclinical NCT research, and anticipated human trials, for epithermal-neutron NCT in the United States. Computational approximations that work well for photon-electron therapy and, to some extent, fast-neutron therapy, are not appropriate for neutron capture therapy. Complete solutions of the transport equations, with an explicit treatment of

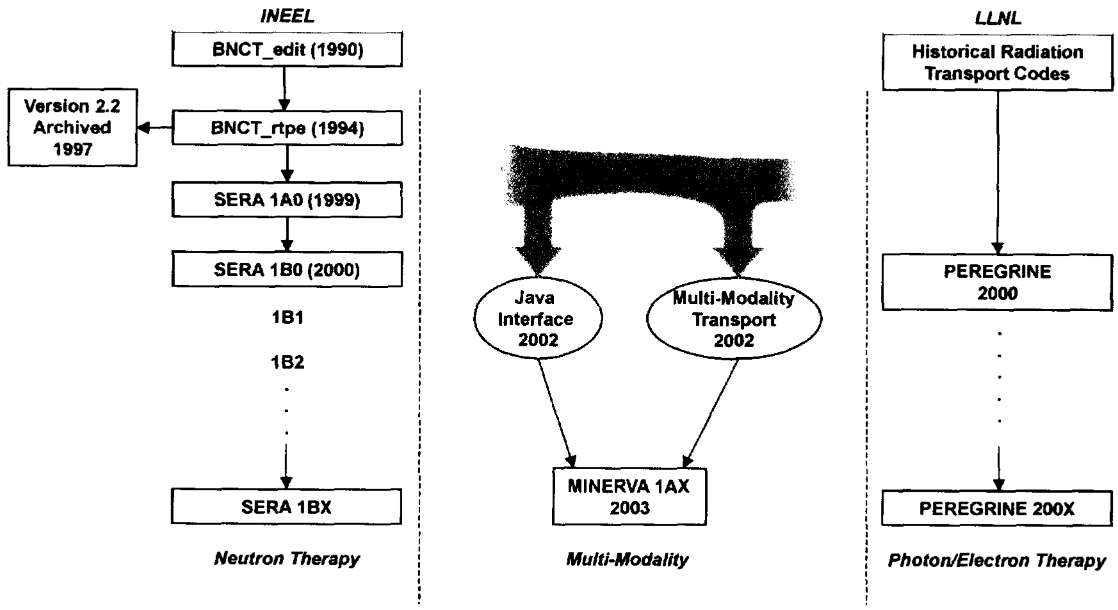

Figure 1. Radiotherapy Planning Software Development at the INEEL and at LLNL.

particle scattering, are required. Standard Monte Carlo radiation transport codes used in other fields of nuclear science, for example MCNP[3], have often been used successfully for this purpose by various investigators. In addition specialized medical image based geometric reconstruction and radiation dose visualization interfaces have been introduced for use with an especially tailored version of MCNP to produce a practical treatment planning system for BNCT[4,5]. Modern three-dimensional general-purpose discrete-ordinates codes have also sometimes been used to perform the necessary calculations[6,7].

However, MCNP and other general-purpose transport codes are designed for very broad applications. They are quite flexible, and have the advantage of dedicated maintenance and quality control by the developers, but in some situations they can tend to be somewhat slow in execution relative to expectations for treatment planning in clinical oncology practice (a few minutes per field, maximum), and there are limitations in the geometric detail that can be modeled. Hence, a project was initiated at the INEEL in 1988 to develop a special-purpose medical image based Monte Carlo system optimized specifically for radiotherapy, with epithermal-neutron boron neutron capture therapy (BNCT) as the first anticipated application. This initial effort, conducted in collaboration with the University of Utah Department of Computer Science, resulted in the BNCT_edit system[8] as shown at the top of Figure 1. BNCT_edit was used by the INEEL in the early 1990's for various preclinical applications, but it was not used for human trials and it was never released for external use.

In 1994 BNCT_edit was replaced by a much-improved system, BNCT_rtpe (BNCT Radiation Treatment Planning Environment). The BNCT_rtpe system was introduced into clinical use in connection with the DOE-sponsored clinical trials of epithermal-neutron BNCT for glioblastoma multiforme that began at Brookhaven National Laboratory in the same year[9]. BNCT_rtpe was developed by the INEEL in collaboration with the Montana State University (MSU) Department of Computer Science. It was based on experience gained with the BNCT_edit development effort in that it featured a sophisticated Non-Uniform Rational B-Spline (NURBS) approach to image modality independent reconstruction of patient geometry from medical images[10].

With this method, the patient anatomy is initially reconstructed in so-called "pixel space," with subsequent rescaling to the actual computational geometry using the true field of view parameters pertinent to the image set. This allows modeling of essentially any anatomy that can be imaged, independent of the image modality, and without any computational restrictions. Furthermore, it incorporated an improved particle tracking method[11] based on a supermposed "edit mesh" that offered relatively rapid computation times (2-4 hours per field on the computer hardware of the time) compared to what had been previously possible, and vastly-improved user interfaces. In addition to the Brookhaven application, BNCT_rtpe was also licensed for use in the European BNCT research programs conducted by the Technical Research Centre of Finland, and by the Commission of the European Communities Joint Research Centre at Petten, in The Netherlands.

Although BNCT_rtpe proved to be a useful and relatively efficient clinical research tool there still was a need to reduce the computation time further, ideally to no more than a few minutes per field. Accordingly, INEEL and MSU undertook some studies in the late 1990s that were focused on achieving a significant breakthrough in execution speed via a total reformulation of the mathematical algorithms. Although it is possible to recast various standard Monte Carlo algorithms for parallel execution on specialized multi-CPU computer systems and thereby achieve increases in execution speed, INEEL and MSU researchers directed their efforts toward development of new and much faster algorithms instead. This approach was taken in recognition of the fact that most radiotherapy research centers and clinics typically operate with single-CPU desktop computer systems. The result of this developmental effort led to the introduction of the completely new SERA[1] treatment planning software in 1998.

The SERA treatment planning system incorporates an integrated method for reconstructing patient geometry from medical images and for subsequently tracking particles through this geometry during a Monte Carlo radiation transport simulation. The method, in contrast to coarse voxel reconstruction methods used with standard transport codes and the NURBS method used in BNCT_rtpe, is based on a pixel-by pixel uniform volume element ("univel") reconstruction of the patient geometry[12]. As with the B-Spline method, construction of the patient geometry is independent of the medical image modality and field of view. Anatomical regions are defined on a selected set of two-dimensional images and these regions are combined to produce a 3-D reconstruction, as shown in Figure 2. Fast scan-line rasterization methods, implemented largely with integer arithmetic, are then used to allow rapid particle tracking through the univel geometry. This is a key distinction between the univel method and standard voxel based reconstruction and tracking methods. Univels along the particle track are investigated and precise intersection points ("distance to boundary" in Monte Carlo terminology) can be rapidly calculated as the particle moves from one anatomical region to the next. Fluxes and doses are then tallied on a superimposed edit mesh in the same manner as in BNCT_rtpe.

The univel method has several attractive features. By scaling the univels to match the resolution of the original image data, the geometric fidelity of the NURBS reconstruction method is retained, but certain numerical difficulties associated with defining non-intersecting volumes in regions where the spline surfaces are very close together are eliminated. Furthermore, and most visibly, the computed fluxes and doses have the same statistical accuracy as with a NURBS model, but the execution time for the transport computations is reduced by a factor of between five and ten. This speedup factor holds even though the new univel model may consist of several million elements. Single-CPU execution times for SERA, with current desktop scientific computing hardware (e.g. 750 MHz Pentium III systems running under Linux), are in the

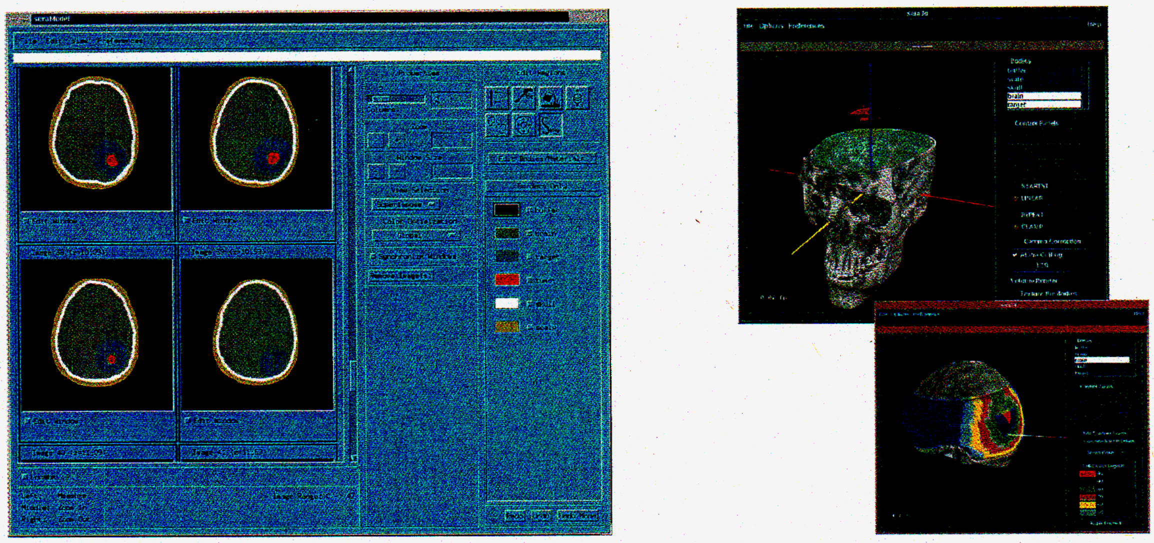

Figure 2. Univel-Based Anatomical Reconstruction in SERA, with three-dimensional dose display.

range of a few minutes per field for neutron applications.

Finally, the basic physics modules of SERA allow incident neutron energies up to 100 MeV, with an explicit (i.e. non-equilibrium) treatment of recoil proton transport[13]. This expands the utility of the SERA system into the field of fast-neutron therapy (FNT), with NCT augmentation[14]. Although other clinically-useful treatment planning methodologies and tools are available for FNT[15], these are based on approximations, whereas SERA offers the capability to rigorously handle the more complex neutron transport and thermalization computations required for combined FNT/NCT applications.

SERA is licensed worldwide for research purposes and is currently in clinical testing in connection with ongoing epithermal-neutron BNCT clinical trials in Finland, Sweden, and in the Netherlands. SERA licensees have agreed to serve as benchmarking and testing institutions for SERA. They have provided, and continue to provide, extremely valuable feedback and suggestions for improvement. SERA is maintained by the INEEL and MSU via an internet-based update distribution. It is anticipated that SERA will be maintained in a reasonably stable configuration for the foreseeable future, as shown on the left-hand side of Figure 1.

II. RECENT ACCOMPLISHMENTS OF LLNL IN THE DEVELOPMENT OF THE PEREGRINE COMPUTATIONAL SYSTEM FOR PHOTON-ELECTRON RADIOTHERAPY

The PEREGRINE dose calculation system[2] is primarily designed to provide Monte Carlo transport calculations fast enough for day-to-day external-beam photon-electron radiation therapy planning, although computations for other types of radiotherapy using specialized versions of PEREGRINE are also possible. It operates on low-cost commodity hardware, enables real time visualization of dose as it is simulated, and completes a full treatment simulation in minutes.

PEREGRINE simulates radiation therapy starting with a set of representative particles randomly sampled from energy, angle, and position distributions determined from offline simulations of the treatment-independent portion of the radiation source. It tracks each photon, electron, and positron through the treatment-dependent beam delivery system and then through the patient using random numbers, microscopic particleinteraction probabilities, and other standard Monte Carlo transport methods. As each particle interacts, it sets in motion other particles that are also tracked. Photons and electrons are tracked to a minimum energy of 10 keV. The minimum energy for delta ray and bremsstrahlung production is 200 keV.

Treatment-specific beam modifiers such as collimators, apertures, blocks, multileaf collimators, and wedges are modeled explicitly during each PEREGRINE calculation. Each component is described in terms of its physical dimensions, material composition, and density. The patient is described as a Cartesian map of material electron density determined from the patient's CT scan. Each CT pixel defines the electron density of a corresponding transport mesh voxel. Material composition is determined from user-defined CT threshold values. Density is determined from a user-defined piecewise-linear function that describes the CT-number-to-density conversion. PEREGRINE records the dose deposited by each particle in a uniform Cartesian dose collection mesh that consists of packed dose-collection spheres.

The PEREGRINE dose calculation system demonstrates the promise of Monte Carlo modeling for photon-electron radiation therapy. The value of stochastic simulations stems from the ability to use basic, microscopic physical data to provide practical information in arbitrarily complex systems. This power is limited only by the computational time necessary to complete sufficiently precise calculations and the creativity of the analyst. Many typical computations can be completed in minutes on hardware designed for clinical treatment planning, and faster computers will allow continued progress.

As is the case with SERA, PEREGRINE is in a relatively mature, stable status. The current release version, recently licensed for commercial applications by the NOMOS Corporation, has been approved by the U.S. Food and Drug Administration (FDA). It is anticipated that PEREGRINE will remain in a stable configuration to facilitate clinical deployment for external beam photon-electron therapy, as shown on the right-hand side of Figure 1.

III. FUTURE DIRECTIONS

With SERA on a path to stabilization, INEEL and MSU began directing their attention to the development of a new generation of radiotherapy planning software, with a much broader range of applications in mind. More or less concurrently, the developers of PEREGRINE were thinking along the same lines. As a result, INEEL, MSU and LLNL launched, in October, 2001, a new project to collaborate in the creation of a multi-modality treatment planning software system that will draw on the combined experience of the two laboratories in their respective areas of interest. It will feature several important new functionalities made possible by recent advances in computational hardware, software, and operating system technology. The objective will be to create an integrated software ~~product~~ system that ~~will be~~is useful for all modern forms of radiotherapy. The new ~~product~~ system will carry the name MINERVA (Modality-Inclusive Environment for Radiotherapeutic Variable Analysis).

Several state of the art features will be incorporated into the new system, which is shown schematically in Figure 3. With the advent of the Java™ internet-based programming language, it is now possible to produce extremely sophisticated software and graphic user interfaces with much greater portability among various computer hardware platforms. In addition, the focus will be on the development of a system that can be easily tailored to any radiotherapy modality (and to include multiple computational methodology options for a given therapeutic modality) via an open "plug-in" based interface environment. The first version of MINERVA will include capabilities for external beam photon, electron and fast-neutron radiotherapy, neutron capture therapy, and molecular targeted radionuclide therapy. Other anticipated additions include new computational modules optimized for external-beam proton therapy, as well as for brachytherapy. Alternate computational methods based on existing transport software such as MCNP could also be incorporated by providing an appropriate

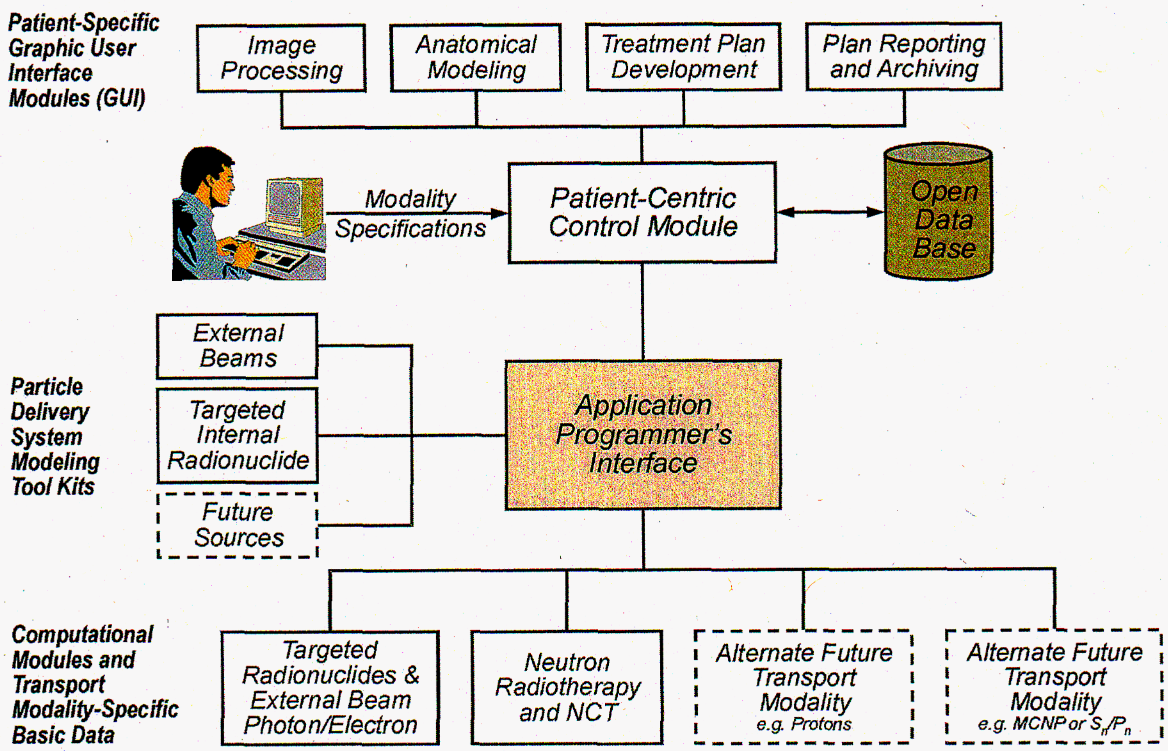

Figure 3. MINERVA – Modality Inclusive Environment for Radiotherapeutic Variable Analysis.

transport specific interface as shown in Figure 3. The new system will be able to ~~be able to~~ employ multi-modality image sets for treatment plan development and it will ~~employ~~ implement a universal data base for patient information file storage (with interfaces to accommodate standard clinical data communication protocols and formats such as RTOG, DICOM-RT, etc.).

~~The objective of the proposed developmental effort will be to produce a system that can be introduced into human trials under the co-sponsorship of the U.S. National Cancer Institute (NCI) or others in the 2004-2005 time frame. Commercial applications may become of interest as the work proceeds, but the primary near-term emphasis will be on research applications.~~

In anticipation of this longer-term joint developmental program, INEEL and LLNL have completed some initial computational feasibility studies for a combined software system. These studies employed an internet-based *ad hoc* coupling of the functionalities in the SERA and PEREGRINE code systems as they currently stand. These initial studies have successfully demonstrated that there should be no fundamental difficulties with the development of the key computational and data interfacing functions that will be required in the new system.

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